May 6, 1952

Dear "Luca" (?)

Your letter of April 28 arrived yesterday. Airmail service from Italy seems relatively slow- I wonder why? I have received letters from Japan usually much faster (3-4 days). I had always understood that you would take the responsibility for the JGM paper [that is, if you accept the sequence of authorship as L C & L for the Genetics paper]. You exaggerate the rawness of your English, even for your letters. It has a continental flavor, but is very legible and quite correct (barring a few minor details). But of course, I'm only an American myself, and no authority on English.

You have raised the question before of the possibility of my attending the international congresses next year. In addition to the Genetics congress, I believe the International Congress of Microbiology is also meeting (in Rome.!) Do you have any affiliation with this group? You mentioned that some sort of special invitation might be fabricated from the Genetics. If this could be done, and possibly the same also for the microbiological congress, I think it might be possible to press the foundations here for some financial support to enable me to attend. If my wife and I did travel to Europe, however, we would prefer to go not merely for the congresses. In addition to our personal plans, would it be feasible for us to spend a few weeks in your laboratory? This is all very tentative, of course.

I am very sorry about the behavior of the last shipment of cultures, and to have wasted so much time. I will rectify this promptly. The silica-gel looked very good for a time, but appears to be too unreliable now. If I recall correctly, you wished to have strains 679, 58, W-1305 and W-1678. I shall send these again, W-1982 and also W-1982 This last is 58-161 lambda-immune, F+. We are also sending this to Hayes to verify whether the UV-stimulation effect depends upon the presence of lambda. Mrs. Lederberg also asks me to send W-1258A, the "prototrophic" NTCC123, and some auxotrophs from it. Although we are not <u>absolutely</u> certain about W-1258A, it is reasonably sure that it is a spontaneous mutant of 123. The F-status is still under study, but probably F-. [Mrs. Gosting here meanwhile has reinvestigated E. coli isolates hitherto regarded as infertile with K-12, W-1177 having been used as the tester. Several of them (still a very few percent of all tested) are fertile with W-1177F+, and must be regarded as self-incompatible]. The only reason for uncertainty about W-1258A is that the mutation occurred in an old culture not under close observation, and we are relying on the correctness of the label. There is very little else in the laboratory that shares its prototrophic, F-, lambdasensitive quality.

I hope this disposes of most of the very old business. Maas' sterility story has been pretty definitely resolved. All of his tests were with Waksman-<u>coli</u> derivatives, and these are all <u>very poorly</u> fertile with K-12 and with each other, although F+. The reported effect of the pantothenate-mutation on fertility is based on incorrect comparisons.

My letter of April 29, which you are possibly reading as I write this, carries some new details on Hfr. I shall refer to it for details.

I would summarize the current status of the Hfr work here as follows:

1) Lac+S^r recombinants from W-1895 (your Hfr recently received) x W-1177.. approach 10% of the total population after two-three hours growth. Recombination is also detectable after negligible growth.

2) The "zygote-colonies" are also detectable as segregating +/- on plain EMB lactose. They show only the same patterns as the Lac+S^r selections. Usually only two components are present: one indistinguishable from the W-1177 parent; the other also Mal-S^r usually Mtl-Xyl-M+B$_1$-TL-, but Lac+ and often V$_6^s$ and V$_1^s$. A few TL+ Lac+ obtained without selection were all V$_1^s$. The results support a linkage sequence V$_6$.Lac.....V$_1$....T..L , as in the earlier data. However, the segregation of TL is not random, but very strongly biassed for TL-, which also perturbs the segregation of the linked factors. The other factors seem to constitute a second group, in which there is a similar perturbation localized at S. From previous experience, this bias can be identified with the elimination or defect for Mal--S, for which F+/F- appears to be decisive. I may add that studies of non-Hfr crosses in which S, M, and Lac have been unselected markers (P- x TL- on methionine-agar) now support a linkage of S--M, but not M--Lac. The latter was previously deduced only from the higher proportion of Lac- in M+ (prototroph) selections of M+Lac- x M-Lac+ but we may now conclude that something else directs the Lac ratio

3) M+TL+ occurs about 2-3% as frequently as the main types already mentioned. It has been noticed without nutritional selection, but studied more thoroughly in diluted platings on minimal agar. The patterns observed are as expected with the selection for TL+. The Lac ratio is difficult to assess, however, because most of the prototrophs are mixed in varying proportions, unlike the standard crosses. I do not understand this unless successive mating is involved.

4) Conditions of high fertility are not very critical. Extremely dilute cultures are capable of mating, and the response is very rapid. Hfr x F- is much more fertile than Hfr x Hfr or Hfr x F+. The progeny of Hfr x Hfr (e.g. Lac+S^r from Lac- x S^r) are still Hfr. However, the productivity of Hfr x Hfr is too low to be very useful for detailed study, although it would be most interesting because of the symmetry. As far as I can tell, the segregation patterns of Hfr x F+ are similar to those of 2) above; I am studying the selected prototrophs more closely.

5) I have started some experiments with azotoiprite (a much more euphonious name than mustard) to new Hfr or F- types. So far (with limited treatments) there has been no success.

6) Cytologically, nothing new. Kliensberger-Nobel has been studying 58-161 x W-1177. She writes about some unique cell forms (not quite L-forms) that she founds only in the cross plates. I have not seen anything spectacular yet with Hfr, but am not sure whether further development of "conjugants?" occurs later on agar.

Hayes has sent a copy of his talk at Oxford. I see we will continue to have semantic problems, which will make it difficult to resolve the issues. The substance of his self-reproducing gamete idea is not illogical (although I think it is certainly poorly stated and probably incorrect). He is suggesting that F+ transduction conveys the same vehicle as is involved in recombination, but empty. Your DNAse experiments may scotch that. The aeration phenocopy, which is reversible, also separates the potential from the actual presence of the F+ agent. His second point, that the gamete is imperfect from the F+ side is no more untenable than my vague idea of elimination after fertilization. I think the occurrence of still hemizygous Mal/S crossovers argues for post-meiotic elimination, but not conclusively. I hope it will be possible to state the issues clearly,in our paper at least. If you could try to repeat his sm-treatment experiments, it would be very useful.